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EXAMINER

HARRIS, ALANA M

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 07/15/2002

AS

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/274,752

Applicant(s)

GOETZL ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 December 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 12-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 and 21-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6, 13</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-11 and 21-26) in Paper No. 19 mailed August 21, 2001 is acknowledged. The traversal is on the ground(s) that Group V (claims 27-31) should also be considered together with Group I. Applicants assert that Group I is drawn to a nucleic acid in an expression vector, transformed into a cell and thus no additional searching burden would be imposed with respect to the invention of Group V. This is found persuasive.

Upon reconsideration claims 27-31 will be joined with Group I. However, the restriction of claims 12-20 of the former restriction is maintained.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-31 are pending.

Claims 12-20, drawn to non-elected inventions are withdrawn from examination.

Claims 1-11 and 21-31 are examined on the merits.

Drawings

3. The drawings are objected to because of reasons cited on attached form PTO 948 completed by draftsman. Correction is required.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

4. **Correction of Informalities -- 37 CFR 1.85**

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

5. **Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Specification

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 6, line 10. Applicant is advised to review the entire disclosure and required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

7. Claims 21 and 27 are objected to under 37 CFR 1.75 as being a substantial duplicate of one another. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 21-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21 and 27-30 contain the recitation "progeny thereof" which is not supported by the specification. Applicants have pointed out that the new claims have support within the specification on pages 16, 17 and 41-56, Examples 2, 3 and 5 in particular. The Examiner has reviewed these pages and has not found support for this recitation. Applicants are advised to pointedly express in the disclosure where the said recitation can be found in order to obviate the instant rejection.

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10. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 broadly claims an isolated nucleic acid encoding an Edg protein that is at least about 85% identical to the amino acid sequence set forth in amino acid sequences, SEQ ID NO:1 and 3 and claim 2 broadly claims the isolated nucleic acid which is at least about 75% identical to the nucleic acid sequence set forth in nucleic acid sequences 2 and 4. The remaining claims include vectors and host cells encompassing the polynucleotide variants of 75% sequence identity and a method of producing these encoded variant proteins, as well as variant polypeptides of 85% sequence identity. The written description in this instant case only sets forth nucleic acids, SEQ ID NO: 2 and 4, which encode polypeptides, SEQ ID NO:1 (Edg4) and 3 (Edg5), respectively. The written description is not commensurate in scope with claims drawn to polynucleotides encoding variant and mutated polypeptides embodied by the listed claims.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO: 1 and SEQ ID NO: 3, the skilled artisan cannot envision the detailed structure or function of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

At the time the application was filed Applicants only had possession of SEQ ID NO: 2 and 4, which encode SEQ ID NO: 1 and 3, respectively and not polypeptides that

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share 85% sequence identity with SEQ ID NO: 1 and 3, nor polynucleotides that share at least 75% sequence identity to SEQ ID NO: 2 and 4. The specification does not evidence the possession of all the nucleic acid molecules encoding possible mutant polypeptides that are capable of acting as G protein-coupled receptors (GPCRs) for lysophospholipids and sphingolipids encoded by endothelial differentiation genes (Edgs), such as wild type Edg4 and Edg5. There is insufficient support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph.

11. Claim 24 is rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of the Tsup-1 human T lymphoblastoma cell line. It is not clear this particular cell line is known and publicly available or can be reproducibly isolated from nature without undue experimentation. Exact replication of a cell line is an unpredictable event. Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the Tsup-1 cell line, a suitable deposit for

patent purposes, evidence of public availability of the cell line or evidence of the reproducibility without undue experimentation of the Tsup-1 cell line, is required.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If deposits are made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the Tsup-1 cell line described in the specification and claims as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

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12. Claims 1, 3 and 6-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 1 is broadly drawn to "[an] isolated nucleic acid encoding an Edg protein that is at least about 85% identical to the amino acid sequence ...SEQ ID NOS: 1, 3" and claim 2 is broadly drawn to "[an] isolated nucleic acid at least about 75% identical to the nucleic acid sequence ...SEQ ID NOS: 2, 4". The specification while being enabling for the polypeptides having the amino acid sequences of SEQ ID NO: 1 and 3, does not reasonably provide enablement for variants that have at least 85% sequence identity. Additionally, the specification is enabled for the polynucleotide sequences, SEQ ID NO: 2 and 4, but not for polynucleotides that are only 75% identical to the said nucleic acid sequences. Applicants have provided examples on pages 9-13 of the specification by which modifications of EDG4 and EDG5 may be produced. However, the specification has yet to evidence that EDG products manufactured by these modifications possess functions that are commensurate with the functions of the native protein. The 85% sequence identical amino acids and 75% sequence identical nucleic acids encoding variant proteins may not maintain the activities proposed in the specification. It would seem that specific function(s) would be required to make the encoded protein useful for the applications disclosed in the specification, such as for treating disorders related to the phospholipid mediators, lysophosphatidic acid (LPA) and sphingosine 1-phosphate

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(S1P) and the prevention of apoptosis, see page 40, lines 12-22. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful. The true fact of the state of the art in peptide chemistry is expressed succinctly in the accompanying Lazar article (Molecular and Cellular Biology 8(3): 1247-1252, March 1988). This article presents data that substantiates the fact that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein.

From the discussion above, it is clear that the predictability of changes to the amino acid sequence is practically nil as far as biological activities are concerned. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acids in a manner reasonably correlated with the broad scope of the claims. Without sufficient guidance, the changes which must be made in the nucleic acid sequences, SEQ ID NO: 2 and 4 and amino acid residues of SEQ ID NO: 1 and 3, which results in less than 100% sequence identity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

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13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 3-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 3 and 4 are vague and indefinite in the recitation "sequence selected.". This is an improper markush group. It is not clear what are the members from the group of amino acid sequences to be selected in view that there are no species set forth. For examination purposes the selected amino acid sequences read on SEQ ID NO: 1 and 3 and the selected nucleic acid sequences read on SEQ ID NO: 2 and 4.

b. Claim 5 is vague and indefinite in the recitation "hybridize under high stringency conditions". While a suggested example of hybridization conditions is provided in the bridging paragraph of pages 7 and 8 of the specification. This example does not non-limiting, accordingly the metes and bounds of the hybridization conditions are not clear.

Claim Rejections - 35 USC § 101

15. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

16. Claims 1-11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, credible or substantial asserted utility or a well established utility.

Applicants have asserted several utilities for the claimed isolated polynucleotides, SEQ ID NO: 2 and 4, their encoded polypeptides, SEQ ID NO: 1 and 3 and variants of said sequences: therapeutics, production of transgenic animals, diagnostic tools and prevention of diseases associated with expression of these sequences, see page 8, lines 22-30; page 24, lines 4-15; bridging paragraph of pages 25 and 26; page 39, lines 22-27 and page 40, lines 12-22. However, these asserted utilities are neither specific nor substantial. The broadly claimed polynucleotides are based on SEQ ID NO: 2 and 4 that allegedly encode novel human membrane protein receptors, members of a subfamily of GPCRs. There is no conclusive information that links expression of SEQ ID NO:2 or 4 to any specific disease state. The mere fact that SEQ ID NO: 1 (Edg4) and SEQ ID NO: 3 (Edg5) have been characterized as GPCRs does not mean that the functions of the polypeptides are synonymous. The specification on page 39, starting at line 22 contemplates the exact mechanism by which Edg receptor proteins play a role in wound healing and angiogenesis, for example.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (Trends in Biotech. 18:34-39, January 2000) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (Genome Research 10:398-400, 2000) states that the error rate of functional annotations in the sequence database is considerable, making it even more

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difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (Trends in Genetics 14:248-250, June 1998) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (Nature Biotechnology 15:1222 and 1223, November 1997) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (Trends in Genetics 15 (4):132-133, April 1999) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Bork et al. (Trends in Genetics 12(10):425-427, October 1996) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Finally, Bowie et al. (Science 247:1306-1310, March 16, 1990) state that determination of three dimensional structure from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (p. 1306). Thus, the specification fails to support the asserted credible, specific and substantial utility of growth factor activity.

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The specification does not disclose a correlation between any specific disorder and an altered level or form of the claimed polynucleotides. Also, the specification does not predict whether the claimed polynucleotides would be overexpressed or underexpressed in a specific, diseased tissue compared to the healthy tissue control. Information provided in the specification is not sufficient to establish that it plays a role in the pathology or etiology of diseases. Accordingly, those skilled in the art cannot rely on this information to implement the processes of treating or preventing a number of types of disorders. The functions of the Edg molecules are not distinctly known and not disclosed in the specification, which speculates merely that these molecules are members of family involved in myriad of disorders. Given the lack of any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it not currently available in practical form the claimed isolated polynucleotides and polypeptides is not credible, substantial or specific.

Claims 1-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, credible or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if Applicants were to evidence that claims 1-11 have a patentable utility they would be enable for the full scope of the invention.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

18. Claims 1-11 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,020,158 (filed May 22, 1997). Sequence 1 (coding region) and sequence 3 (cDNA) of U.S. Patent #6,020,158 disclose isolated nucleic acids encoding Edg4 protein that is at least about 85% identical to the amino acid sequence consisting of SEQ ID NO: 1, see attached database sheets. These isolated nucleic acid sequences are at least about 75% identical to Applicants' SEQ ID NO: 2 and will hybridize under high stringency conditions to the nucleic acid complement of a sequence consisting of

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SEQ ID NO: 2. The patent sets forth in column 5, lines 17-32 that nucleotide sequences of expression vectors may be joined to the disclosed nucleotide sequences, as well as control sequences such as promoters or enhancers, see column 14, lines 53-58. Example 4 of the patent, columns 13-15 list a number of expression host cells that may be transfected or transformed by expression vectors, which provide for the expression of the Edg protein through standard culture methods, see bridging paragraphs of columns 7 and 8; 14 and 15.

19. Claims 1, 3 and 5-11 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 5,856,443 (filed December 6, 1996). Patent #5,856,443 discloses sequence 1, an isolated nucleic acid encoding the Edg5 protein (SEQ ID NO: 3).

Nucleic acid sequence 1 encodes the protein set forth in the patent as sequence 2 which is at least about 85% identical to the amino acid sequence consisting of SEQ ID NO: 3, see attached database sheets. The disclosed nucleic acid will hybridize under high stringency conditions to the nucleic acid complement of a sequence consisting of SEQ ID NO: 4. Furthermore, the patent sets forth in column 6, lines 22-28 and lines 46-64 that the disclosed nucleotide sequences may be inserted in a cloning vector for the expression of the polypeptide encoded by the polynucleotide sequence. The said sections of the patent also list a number of expression host cells that may be transfected or transformed by expression vectors, which provide for the expression of the Edg protein through standard culture methods well known in the art see column 7, lines 5-14.

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20. Claims 1, 3 and 5-9 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Accession number AA419064, clone 755526 (May 12, 1997/ IDS Reference 2, Paper 13). This reference as well as the accompanying sequence alignment sheets, labeled "genealign.rec" discloses an isolated nucleic acid encoding an Edg protein that is at least about 85% identical to the amino acid sequence of SEQ ID NO: 1 and an isolated nucleic acid which will hybridize under high stringency conditions to the nucleic acid complement of SEQ ID NO: 2. This reference continues to disclose a pT7T3D plasmid containing a polylinker, as well as a host cell, DH10B.

21. Claims 1-5 rejected under 35 U.S.C. 102(b) as being anticipated by MacLennan et al. (Molecular and Cellular Neurosciences 5:201-206, 1994). MacLennan discloses an isolated nucleic acid encoding the Edg5 protein that is at least about 85% identical to SEQ ID NO: 3, see page 204, Figure 2 and attached database sheets. The said nucleic acid is at least 75% identical to the nucleic acid sequence consisting of SEQ ID NO: 4, see page 202, Figure 1 caption on page 203 and database sheets. The disclosed isolated nucleic acid would hybridize under high stringency conditions to the nucleic acid complement of a sequence consisting of SEQ ID NO: 4.

22. Claims 1-3 and 5-11 are rejected under 35 U.S.C. 102(a) as being anticipated by An et al. (April 3, 1998/ IDS Reference 3, Paper 6). An discloses an Edg4 protein that is at least about 85% identical to SEQ ID NO: 1 (see page 7907, column 2, Fig. 1 and accompanying database sheet, Accession number AF011466, July 29, 1998). The

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nucleic acid that encodes the disclosed Edg4 protein is disclosed on the attached database sheet. As noted on page 7906, column 1 in the footnotes section, "The nucleotide sequence(s) reported ...has been submitted...with accession number(s) AF011466." The said isolated nucleic acid that encodes the Edg4 protein is at least about 75% identical to SEQ ID NO: 2 (see attached database sheet). This isolated nucleic acid will hybridize under high stringency conditions to the nucleic acid complement of SEQ ID NO:2.

The isolated nucleic acid was subcloned into the mammalian expression vector pCDEF3 and the resulting expression construct was designated Edg4/EF3, see page 7907, col. 1, Cloning and Plasmid...section. SRE luciferase reporter gene plasmids were constructed and Jurkat T cells were co-transfected with the said reporter plasmid in combination with Edg4/EF3 (page 7907, col. 1, Reporter Gene Assay Section). The host cells were cultured under conditions suitable for the expression of an Edg protein as indicated in the Reporter Gene Assay Section and stated on page 7907, col. 2, second full paragraph.

23. Claims 21-31 are free of the art.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Alana M. Harris, Ph.D.

July 1, 2002